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## Memorandum

To: Trialists

Fr: Curtis Meinert

Re: On reasons why DSMBs should not be masked

The primary duty of a DSMB is to review treatment results over the course of a trial for the purpose of making recommendations to the investigator group and sponsor as to whether the trial should continue unaltered. Typically, they do this by looking at data reports generated by the coordinating center on designated time schedules (e.g., every six month intervals) or after specified landmarks events in the trial (e.g., after specified numbers of primary events in the trial). Data reports may be masked or unmasked.

Suppose a trial of Wonder Drug and a corresponding control treatment. The columns in monitoring reports for unmasked DSMBs would be labeled WonD and Ctrl within and across reports.

If the report is masked, columns would be labeled “A” and “B” without indication of which is which. The labeling may be the same over time or vary from report to report, for example, with “A” designating the control treatment in one report and the study treatment in another report. The masking robs monitors of “memory” regarding data trends because they have no way of comparing over time because results for “B” in one report may be designated “A” in the next report.

I have yet to run into a study investigators who believes masking DSMBs is a good idea. That being so why then is it practiced? Primarily because sponsors and DSMBs think it is a good idea. *Why not mask? It cannot hurt. The masking will add to the aura of credibility and, besides, the mask can be lifted at any time during the trial if necessary.*

I wrote a piece entitled *Masked monitoring in clinical trials - Blind stupidity?* (NEJM 1998; 338:1,381-1,382) years back. I have not mellowed over time.

One can question the masking on ethical grounds. *Is it proper to conduct a trial where no one sees interim results by treatment group? Is the practice consistent with the expectation of persons enrolled to be protected from harm?*

My primary objection to the masking is its degrading effect on the monitoring process. The masking has a stultifying effect on dialogue among members of the DSMB. Even if a person believes he/she knows the treatment represented by the code, that person has to pretend to not know so as to keep other members in the dark regarding treatment.

The masking is a distraction because people are invariably driven to “break the code”. I remember years ago sitting as a DSMB member for an eye trial. Eventually the mask was lifted. The ophthalmologist said he knew the treatment group virtually from day one because of a particular characteristic unique to the test treatment. I was too dumb to have noticed.

Treatments are like bullets fired from guns. Every gun leaves unique marks on bullets fired from it. Likewise, every treatment has its own unique characteristics. This means that characteristics unique

to a treatment, like side effects and laboratory results, cannot be presented in the masked portion of monitoring reports in order to preserve the mask. As a result the coordinating center has to prepare two reports; one in which treatment groups are masked and another in which they are not; complicating production and increasing the probability of error and mixups in producing reports.

It also means that if the DSMB requests additional analyses to explore an emerging trend or peculiarities the coordinating has to carry out two sets of analyses -- one assuming the trend or peculiarity is associated with the test treatment and another assuming it is associated with the control treatment.

A gambit to convince skeptics to accept masking is that it can be lifted if need be. True, but experience teaches that the debate whether to unmask can be contentious and may go on over several meetings before the mask is actually lifted.

A variation on masking is one where DSMB members are provided with sealed envelopes containing the masking key allowing individual members to unmask themselves; typically announced. The obvious problem is the awkwardness of conversations if some members are masked and others are not.

Another variation is where reports are masked but where the masking is revealed prior to meetings of the DSMB. The purpose is to safeguard results if reports are lost or seen by others. The downside is that the masking makes reports less reader friendly and increases the chances of confusion if members mixup the codes.

So there are the reasons why I have not mellowed with age.